## (19) World Intellectual Property Organization International Bureau

(43) International Publication Date 4 August 2005 (04.08.2005)

## (10) International Publication Number WO 2005/070883 A1

C07C 317/46, (51) International Patent Classification7: A61K 31/04, A61P 29/00, 9/00

(21) International Application Number:

PCT/CA2005/000083

(22) International Filing Date: 25 January 2005 (25.01.2005)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 60/539,666

27 January 2004 (27.01.2004)

(71) Applicant (for all designated States except US): MERCK FROSST CANADA & CO. [CA/CA]; 16711 Trans-Canada Highway, Kirkland, Québec H9H 3L1 (CA).

(72) Inventors; and

(75) Inventors/Applicants (for US only): DUFRESNE, Claude [CA/CA]; 16711 Trans-Canada Highway, Kirkland, Québec H9H 3L1 (CA). BERTHELETTE, Carl [CA/CA]; 16711 Trans-Canada Highway, Kirkland, Québec H9H 3L1 (CA). LI, Lianhai [CA/CA]; 16711 Trans-Canada Highway, Kirkland, Québec H9H 3L1 (CA). GUAY, Daniel [CA/CA]; 16711 Trans-Canada Highway, Kirkland, Québec H9H 3L1 (CA). GALLANT, Michel [CA/CA]; 16711 Trans-Canada Highway, Kirkland, Ouébec H9H 3L1 (CA). LACOMBE, Patrick [CA/CA]; 16711 Trans-Canada Highway, Kirkland, Québec H9H 3L1 (CA), ASPIOTIS, Renee [CA/CA]; 16711 Trans-Canada Highway, Kirkland, Québec H9H 3L1 (CA). WANG, Zhaoyin [CA/CA]; 16711 Trans-Canada Highway, Kirkland, Quéhec H9H 3L1 (CA). STURINO, Claudio, F. [CA/CA]; 16711 Trans-Canada Highway, Kirkland, Québec H9H 3L1 (CA).

(74) Agent: OGILVY RENAULT; Suite 1600, 1981 McGill College Avenue, Montréal, Québec H3A 2Y3 (CA).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

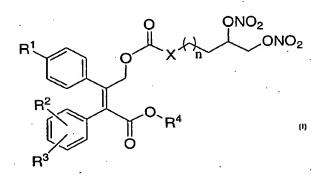
(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM. KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: NITRIC OXIDE RELEASING PRODRUGS OF DIARYL-2-(5H)-FURANONES AS CYCLOOXYGENASE-2 INHIBITORS



The invention encompasses novel (57) Abstract: compounds of Formula I, which are nitric oxide-releasing prodrugs of diaryl-2-(5H)-furanones useful in the treatment of cyclooxygenase-2 mediated diseases. Formula (I). The invention also encompasses certain pharmaceutical compositions and methods for treating cyclooxygenase-2 mediated diseases comprising the use of compounds of Formula 1. The above compounds may be used as a combination therapy with low-dose aspirin to treat chronic cyclooxygenase-2 mediated diseases or conditions while also reducing the risk of thrombotic cardiovascular events.